Steven Shak, M.D.

Chief Medical Officer
Genomic Health, Inc.
301 Penobscot Drive
Redwood City, CA 94063
(650) 569-2251 (phone) (650) 444-4432 (cell)
(650) 556-1132 (fax)
sshak@genomichealth.com (e-mail)

Professional Appointments:

2000-	Chief Medical Officer and Co-Founder, Genomic Health, Inc.
2007-	Board of Directors, Cystic Fibrosis Foundation
2005-	Board of Directors, Cystic Fibrosis Foundation Therapeutics, Inc
2004-	Genomic Health Laboratory Director for NY State
2000-04	Board of Directors, Genomic Health, Inc.
1999-	Board of Directors, The Children's Cause for Cancer Advocacy
1998-00	Senior Director, Medical Affairs, Genentech, Inc. Headed Pulmonary Therapeutic Unit, Epidemiology, Health Care Economics and Medical Information
1998-00	Staff Clinical Scientist, Genentech, Inc.
1996-98	Senior Clinical Scientist, BioOncology, Genentech, Inc.
1989-96	Research Director, Departments of Immunobiology, Pulmonary Research, and Pathology, Genentech, Inc.
1986-89	Research Scientist, Genentech, Inc.
1984-86	Assistant Professor of Medicine and Pharmacology, New York University School of Medicine

Key Genomic Health Accomplishments 2000-:

- Led Clinical Development Program for Oncotype DX®
  - Performed three breast cancer clinical trials to develop the 21 gene panel and Recurrence Score algorithm
  - Successfully completed large pivotal trials with NSABP and Kaiser Permanente to validate Oncotype DX as a predictor of the likelihood of distant recurrence and chemotherapy benefit in women with node negative breast cancer
- Established Medical Organization
  - Comprises team of professionals with excellence in trial design, biostatistics and bioinformatics, oncology, pathology, and clinical trial operations

Key Genentech Accomplishments 1986-2000:

- Led Herceptin Clinical Team
  - Directed worldwide Phase III clinical trials demonstrating survival advantage of the anti-HER2 antibody that targets a specific genetic alteration in breast cancer
  - Presented Herceptin clinical trial results to FDA Oncology Drug Advisory Committee
  - Collaborated with DAKO to get FDA approval of the Herceptest for tumor HER2 overexpression
  - Optimized clinical trial management and data flow, leading to approval 1 year earlier than anticipated
- Discovered Pulmozyme and Led Pulmozyme Project Team
  - Cloned human DNase I gene and developed the first new treatment in 30 years for the genetic disease, Cystic Fibrosis
  - Obtained worldwide regulatory approval in 5 years
  - Ensured patient access to Pulmozyme regardless of ability to pay, serving on Board of Directors, Genentech Endowment for Cystic Fibrosis
- Initiated Clinical Development of Angiogenesis Inhibitor, Avastin
  - Streamlined IND filing and initiated the first Phase I trial
  - Worked with oncologists to create new clinical development strategy for anti-VEGF antibody
- Assessed and Prioritized Genentech R & D Efforts to Increase Company Value
  - Chair, Clinical Assessment Committee and Opportunistic Therapeutic Area Team
  - Member, Research and Clinical Review Committees
- Partnered with Patient Advocates and Legislators
  - Collaborated with leading organizations, including Cystic Fibrosis Foundation and National Breast Cancer Coalition
  - Lobbied Congress on behalf of patients and biotech industry
  - Managed Herceptin Expanded Access Program

Education and Postdoctoral Training:

1981-84	Postdoctoral Research, University of California, San Francisco, Cardiovascular Research Institute, Rosalyn Russell Arthritis Research Laboratory
1980-84	Pulmonary Fellowship, University of California, San Francisco, Cardiovascular Research Institute
1977-80	Internal Medicine Internship and Residency, Bellevue Hospital, New York
1973-77	M.D., New York University School of Medicine
1969-73	B.A., Amherst College

Certification and Licensure:

2003	Member, American Society of Clinical Oncology
1982	Diplomate, Pulmonary Disease
1980	Diplomate, American Board of Internal Medicine
1980	Licensed, California
1978	Licensed, New York State

Honors and Awards:

2001	NYU Biotechnology Award
1995	Prix Gallien, Portugal for "Pulmozyme Discovery"
1995	"Parenting Achievement Award," Parenting Magazine
1993	Distinguished Corporate Scientist Award, Cystic Fibrosis Foundation
1992	CF Achievement Award, Cystic Fibrosis Research, Inc.
1985	J. Burns Amberson Award, NY Lung Association
1980	Medical School Pulmonary Faculty Training Award, NIH
1977	Alpha Omega Alpha
1974	Valentine Mott Award in Anatomy and Cell Biology
1973	Summa Cum Laude
1973	Phi Beta Kappa
1973	Sigma Xi
1973	Howard Waters Doughty Prize in Chemistry

Publications:

I. Book Chapters.

1. S SHAK. Mucins and lung secretions. In THE LUNG--SCIENTIFIC FOUNDATIONS. (RG Crystal, JB West, ER Weibel, and PJ Barnes, eds.) Lippincott-Raven Publishers, Philadelphia, pp. 479-486, 1997.

2. Goldstein IM, SHAK S. Host defenses in the lung: Neutrophils, complement, and other humoral mediators. In TEXTBOOK OF RESPIRATORY MEDICINE. (JF Murray and JA Nadel, eds.) W.B. Saunders Company, Philadelphia, pp. 402-418, 1994.

3. Goldstein IM, SHAK S. Humoral and cellular mediators of host defenses. In TEXTBOOK OF RESPIRATORY MEDICINE. (JF Murray and JA Nadel, eds.) W.B. Saunders Company, Philadelphia, pp. 358-373, 1988.

4. SHAK S. Molecular mechanisms for the catabolism of leukotriene B_4. In ADVANCES IN INFLAMMATION RESEARCH. Vol. 12. (A Lewis, ed.) Raven Press, Ltd., New York, pp. 111-124, 1988.

5. SHAK S. Leukotriene B_4 catabolism: Quantitation of leukotriene B_4 and its ω-oxidation prducts by reversed phase high-performance liquid chromatography. METHODS IN ENZYMOLOGY. Vol. 141. Cellular Regulators (AR Means and PM Conn, eds.) Academic Press, Florida, pp. 355-371, 1987.

6. SHAK S, Goldstein IM. The major pathway for leukotriene B_4 catabolism in human polymorphonuclear leukocytes involves ω-oxidation by a cytochrome P-450 enzyme. In PROSTAGLANDINS, LEUKOTRIENES, AND LIPOXINS. (JM Bailey, ed.) Plenum Publishing Corporation, New York, 1985.

II. Articles

1. Goldstein LJ, Gray R, Badve S, Childs BH, Yoshizawa C, Rowley S, SHAK S, Baehner FL, Ravdin PM, Davidson NE, Sledge GW Jr, Perez EA, Shulman LN, Martino S, Sparano JA. Prognostic utility of the 21-gene assay in hormone receptor-positive operable breast cancer compared with classical clinicopathologic features. THE JOURNAL OF CLINICAL ONCOLOGY. 26(25):4063-71, 2008

2. Badve SS, Baehner FL, Gray RP, Childs BH, Maddala T, Liu ML, Rowley SC, SHAK S, Perez ED, Shulman LJ, Martino S, Davidson NE, Sledge GW, Goldstein LJ, Sparano JA. Estrogen- and progesterone-receptor status in ECOG 2197: Comparison of immunohistochemistry by local and central laboratories and quantitative reverse transcription polymerase chain reaction by central laboratory. THE JOURNAL OF CLINICAL ONCOLOGY. 20;26(15):2473-81, 2008.

3. Chang JC, Makris A, Gutierrez MC, Hilsenbeck SG, Hackett JR, Jeong J, Liu ML, Baker J, Clark-Langone K, Baehner FL, Sexton K, Mohsin S, Gray T, Alvarez L, Chamness GC, Osborne CK, SHAK S. Gene expression patterns in formalin-fixed, paraffin-embedded core biopsies predict docetaxel chemosensitivity in breast cancer patients. BREAST CANCER RESEARCH AND TREATMENT. 108:233-40, 2008.

4. Habel LA, SHAK S, Jacobs MK, Capra A, Alexander C, Pho M, Baker J, Walker M, Watson D, Hackett J, Blick NT, Greenberg D, Fehrenbacher L, Langholz B, Quesenberry CP. A population-based study of tumor gene expression and risk of breast cancer death among lymph node-negative patients. BREAST CANCER RESEARCH. 8:R25, 2006.

5. Paik S, Tang G, SHAK S, Kim C, Baker J, Kim W, Cronin M, Baehner FL, Watson D, Bryant J, Costantino JP, Geyer CE Jr, Wickerham DL, Wolmark N. Gene expression and benefit of chemotherapy in women with node-negative, estrogen receptor-positive breast cancer. THE JOURNAL OF CLINICAL ONCOLOGY. 10;24(23):3726-34, 2006.

6. Cobleigh MA, Tabesh B, Bitterman P, Baker J, Cronin M, Liu ML, Borchik R, Mosquera JM, Walker MG, SHAK S. Tumor gene expression and prognosis in breast cancer patients with 10 or more positive lymph nodes. CLINICAL CANCER RESEARCH. 11:8623-31, 2005.

7. Gianni L, Zambetti M, Clark K, Baker J, Cronin M, Wu J, Mariani G, Rodriguez J, Carcangiu M, Watson D, Valagussa P, Rouzier R, Symmans WF, Ross JS, Hortobagyi GN, Pusztai L, SHAK S. Gene expression profiles in paraffin-embedded core biopsy tissue predict response to chemotherapy in women with locally advanced breast cancer. THE JOURNAL OF CLINICAL ONCOLOGY. 23:7265-77, 2005.

8. Jain A, Tindell CA, Laux I, Hunter JB, Curran J, Galkin A, Afar DE, Aronson N, SHAK S, Natale RB, Agus DB. Epithelial membrane protein-1 is a biomarker of gefitinib resistance. PROCEEDINGS OF THE NATIONAL ACADAMY OF SCIENCES U S A. 102:11858-63, 2005.

9. Esteva FJ, Sahin AA, Cristofanilli M, Coombes K, Lee SJ, Baker J, Cronin M, Walker M, Watson D, SHAK S, Hortobagyi GN. Prognostic role of a multigene reverse transcriptase-PCR assay in patients with node-negative breast cancer not receiving adjuvant systemic therapy. CLINICAL CANCER RESEARCH. 11:3315-9, 2005.

10. Paik S, SHAK S, Tang G, Kim C, Baker J, Cronin M, Baehner FL, Walker MG, Watson D, Park T, Hiller HT, Fisher ER, Wickerham DL, Bryant J, Wolmark N. A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer. THE NEW ENGLAND JOURNAL OF MEDICINE. 351:2817-2826, 2004.

11. Cronin M, Pho M, Dutta D, Stephans JC, SHAK S, Kiefer MC, Esteban JM, Baker JB. Measurement of gene expression in archival, paraffin-embedded tissues: Development and performance of a 92-gene reverse transcriptase-polymerase chain reaction assay. AMERICAN JOURNAL OF PATHOLOGY. 164:35-42, 2004.

12. Vogel CL, Cobleigh MA, Tripathy D, Gutheil JC, Harris LN, Fehrenbacher L, Slamon DJ, Murphy M, Novotny WF, Burchmore M, SHAK S, Stewart SJ, Press M. Efficacy and safety of trastuzumab as a single agent in first-line treatment of HER2-overexpressing metastatic breast cancer. JOURNAL OF CLINICAL ONCOLOGY. 20:719-26, 2002.

13. Seidman A, Hudis C, Pierri MK, SHAK S, Paton V, Ashby M, Murphy M, Stewart SJ, Keefe D. Cardiac dysfunction in the trastuzumab clinical trials experience. JOURNAL OF CLINICAL ONCOLOGY. 20:1215-21, 2002.

14. Vogel CL, Cobleigh MA, Tripathy D, Gutheil JC, Harris LN, Fehrenbacher L, Slamon DJ, Murphy M, Novotny WF, Burchmore M, SHAK S, and Stewart SJ. First-line Herceptin monotherapy in metastatic breast cancer. ONCOLOGY. 61:S37-42, 2001.

15. Gordon MS, Margolin K, Talpaz M, Sledge GW, Holmgren E, Benjamin R, Stalter S, SHAK S, and Adelman D. A Phase I safety and pharmacokinetic study of recombinant human anti-vascular endothelial growth factor in patients with advanced cancer. JOURNAL OF CLINICAL ONCOLOGY. 19:843-850, 2001.

16. Slamon DJ, Leyland-Jones B, SHAK S, Fuchs HJ, Paton V, Bajamonde A, Fleming T, Eiermann E, Wolter JD, Pegram M, Baselga J, and Norton LA. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. THE NEW ENGLAND JOURNAL OF MEDICINE 344:783-792, 2001.

17. Cipolla DC, Gonda I, SHAK S, Kovesdi I, Crystal R, and Sweeney TD. Coarse spray delivery to a localized region of the pulmonary airways for gene therapy. HUMAN GENE THERAPY 11:361-71, 2000.

18. Cobleigh M, Vogel CL, Tripathy D, Robert NJ, Scholl S, Fehrenbacher L, Wolter JM, Paton V, SHAK S, Lieberman L, and Slamon DJ; Multinational study of the efficacy and safety of humanized anti-HER2 monoclonal antibody in women who have HER2-overexpressing metastatic breast cancer that has progressed after chemotherapy for metastatic disease. JOURNAL OF CLINICAL ONCOLOGY 17:2639, 1999.

19. SHAK S, Baughman SA, Curd JG, Fuchs HA, Perry C, Teeter G, Leber L. Genentech and breast cancer advocacy. BREAST DISEASE 10:61-64, 1998.

20. SHAK S for the Herceptin Multinational Investigator Study Group: Overview of the trastuzumab (Herceptin) anti-HER2 monoclonal antibody clinical program in HER2-overexpressing metastatic breast cancer. SEMINARS IN ONCOLOGY. 26(suppl 12):71-77, 1999.

21. Harvey B, Leopold PL, Hackett NR, Grasso TM, Williams PM, Tucker A, Kaner RJ, Ferris B, Gonda I, Ramalingam R, Kovesdi I, SHAK S, Crystal R. Airway epithelial expression of vector-derived cystic fibrosis transmembrane conductance regulator (CFTR) mRNA transcripts following repetitive endobronchial spray administration of an adenovirus vector expressing the normal CRTR cDNA to individuals with cystic fibrosis. JOURNAL OF CLINICAL INVESTIGATION. 104:1245-1255, 1999.

22. Ulmer JS, Herzka A, Toy KJ, Baker DL, Dodge AH, Sinicropi D, SHAK S, Lazarus RA. Engineering Actin Resistant Human DNase I for Treatment of Cystic Fibrosis. PROCEEDINGS NATIONAL ACADEMY OF SCIENCE, USA. 93:8225-8229, 1996.

23. Macanovic M, Sinicropi D, SHAK S, Baughman S, Thiru S, Lachmann PJ. The treatment of systemic lupus erythematosus (SLE) in NZB/W F1 hybrid mice; studies with recombinant murine DNase and with dexamethasone. CLINICAL AND EXPERIMENTAL IMMUNOLOGY. 106:243-252, 1996.

24. Puchelle E, Zahm JM, de Bentzmann S, Grosskopf C, SHAK S, Mougel D, Polu JM. Effects of rhDNase on purulent airway secretions in chronic bronchitis. EUROPEAN RESPIRATORY JOURNAL. 9:765-9, 1996.

25. Zahm JM, Girod de Bentzmann S, Deneuville E, Perrot-Minnot C, Dabadie A, Pennaforte F, Roussey M, SHAK S, Puchelle E. Dose-dependent in vitro effect of recombinant human DNase on rheological and transport properties of cystic fibrosis respiratory mucus. EUROPEAN RESPIRATORY JOURNAL. 8:381-6, 1995.

26. SHAK S. Aerosolized recombinant human DNase I for the treatment of cystic fibrosis. CHEST 107:65S-70S, 1995.

27. Sinicropi D, Baker DL, Prince WS, Shiffer K, SHAK S. Colorimetric determination of DNase I activity with a DNA-methyl green substrate. ANALYTICAL BIOCHEMISTRY. 222:351-358, 1994.

28. Chamow SM, Kogan TP, Venuti M, Gadek T, Harris RJ, Peers DH, Mordenti J, SHAK S, Ashkenazi A. Modification of CD4 immunoadhesin with monomethoxypoly(ethylene glycol) aldehyde via reductive alkylation. BIOCONJUGATE CHEMISTRY. 5:133-140, 1994.

29. Ranasinha C, Assoufi B, SHAK S, Christiansen D, Fuchs H, Empey D, Geddes D, Hodson M. Efficacy and safety of short-term administration of aerosolised recombinant human DNase I in adults with stable stage cystic fibrosis. THE LANCET. 342:199-202, 1993.

30. Ramsey BW, Astley SJ, Aitken ML, Burke W, Colin AA, Dorkin HL, Eisenberg JD, Gibson RL, Harwood IR, Schidlow DV, WilmottRW, Wohl ME, Myerson LJ, SHAK S, Fuchs H, Smith AL. Efficacy and safety of short-term administration of aerosolized recombinant human deoxyribonuclease in patients with cystic fibrosis. AMERICAN REVIEW OF RESPIRATORY DISEASE. 148:145-151, 1993.

31. Hubbard RC, McElvaney NG, Birrer P, SHAK S, Robinson WW, Jolley C, Wu M, Chernick MS, Crystal RG. A preliminary study of aerosolized recombinant human deoxyribonuclease I in the treatment of cystic fibrosis. THE NEW ENGLAND JOURNAL OF MEDICINE. 326:812-815, 1992.

32. Aitken ML, Burke W, McDonald G, SHAK S, Montgomery AB, Smith A. Recombinant human DNase inhalation in normal and patients with cystic fibrosis: A phase I study. THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. 267:1947-1951, 1992.

33. SHAK S, Capon DJ, Hellmiss R, Marsters SA, Baker CL. Recombinant human DNase I reduces the viscosity of cystic fibrosis sputum. PROCEEDINGS OF THE NATIONAL ACADAMY OF SCIENCES, USA. 87:9188-9192, 1990.

34. SHAK S, Davitz MA, Wolinsky ML, Nussenzweig V, Turner MJ, Gurnett A. Partial characterization of the cross reacting determinant, a carbohydrate epitope shared by decay accelerating factor (DAF) and the variant surface glycoprotein (VSG) of the african Trypanosoma brucei. THE JOURNAL OF IMMUNOLOGY. 140:2046-2050, 1988.

35. Davitz MA, Hereld D, SHAK S, Krakow JL, Englund PT, Nussenzweig V. A glycan-phosphatidylinositol-specific phospholipase D in human serum. SCIENCE. 238:81-4, 1987.

36. Kruskal BA, SHAK S, Maxfield FR. Spreading of human neutrophils is immediately preceded by a large increase in cytoplasmic free calcium concentration. PROCEEDINGS OF THE NATIONAL ACADEMY OF THE SCIENCES USA. 83:2919-2923, 1986.

37. SHAK S, Goldstein IM. The leukotriene B_4 ω-hydroxylase in human polymorphonuclear leukocytes is a membrane-associated, NADPH-dependent cytochrome P-450 enzyme. TRANSACTIONS OF THE ASSOCIATION OF AMERICAN PHYSICIANS. 48:352-360, 1985.

38. SHAK S, Goldstein IM. Leukotriene B4 ω-hydroxylase in human polymorphonuclear leukocytes: Partial purification and identification as a cytochrome P-450. THE JOURNAL OF CLINICAL INVESTIGATION. 76:1218-1228, 1985.

39. SHAK S, Reich N, Goldstein IM, Ortiz de Montellano PM. Leukotriene B_4 ω-hydroxylase in human polymorphonuclear leukocytes: Suicidal inactivation by acetylenic fatty acids. THE JOURNAL OF BIOLOGICAL CHEMISTRY. 260:13023-13028, 1985.

40. SHAK S, Goldstein IM. Carbon monoxide inhibits ω-oxidation of leukotriene B_4 by human polymorphonuclear leukocytes: Evidence that catabolism of leukotriene B_4 is mediated by a cytochorme P-450 enzyme. BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS. 123:475-481, 1984.

41. SHAK S, Goldstein IM. ω-Oxidation is the major pathway for the catabolism of leukotriene B_4 in human polymorphonuclear leukocytes. THE JOURNAL OF BIOLOGICAL CHEMISTRY. 259:10181-10187, 1984.

42. Perez HD, Roll JF, Bissell DM, SHAK S, Goldstein IM. Ethanol induces isolated rat hepatocytes to generate chemotactic activity for polymorphonuclear leukocytes. THE JOURNAL OF CLINICAL INVESTIGATION. 74:1350-1357, 1984.

43. Charo, IF, SHAK S, Darasek MA, Davison PM, Goldstein IM. Prostaglandin I_2 is not a major metabolite of arachidonic acid in cultured endothelial cells from human foreskin microvessels. THE JOURNAL OF CLINICAL INVESTIGATION. 74:914-919, 1984.

44. Perez HD, Bissell DM, Roll FJ, SHAK S, Goldstein IM. A possible explanation for leukocytic infiltration of the liver in acute alcoholic hepatitis: Ethanol-induced generation by hepatocytes of a lipid chemotactic factor. TRANSACTIONS OF THE ASSOCIATION OF AMERICAN PHYSICIANS. 96:56-64, 1983.

45. SHAK, S, Perez HD, Goldstein IM. A novel dioxygenation product of arachidonic acid posseses potent chemotactic activity for human polymorphonuclear leukocytes. THE JOURNAL OF BIOLOGICAL CHEMISTRY, 258:14948-14953, 1983.